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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/574,967

05/24/2007

Jonathan Miles Brown

2833-113

5906

6449

7590

09/16/2010

ROTHWELL, FIGG, ERNST & MANBECK, P.C.

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WASHINGTON, DC 20005

EXAMINER

AUDET, MAURY A

ART UNIT

PAPER NUMBER

1654

NOTIFICATION DATE

DELIVERY MODE

09/16/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No. 10/574,967	Applicant(s) BROWN ET AL.	
	Examiner MAURY AUDET	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-20 is/are pending in the application.
- 4a) Of the above claim(s) 4,5 and 12-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3 and 6-11 is/are rejected.
- 7) ☒ Claim(s) 1, 3, and 6-11 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See cont. sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

IDS's: 10/11/06, 12/27/07, 12/28/07, 7/6/10

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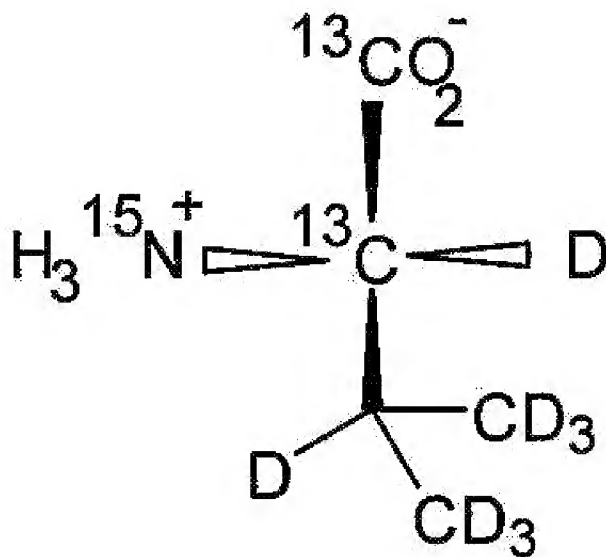
DETAILED ACTION

The present application is a national stage of PCT/US04/32941.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1, 3 and 6-11, and the elected compound of the invention (chemical name & structure below) and compositions comprising the same of:

1, 2- $^{13}\text{C}_2$, ^{15}N , $^2\text{H}_8$ -L-Valine



in the reply filed on 7/6/10 is acknowledged.

In the Restriction Requirement, lack of unity was established based on Anderson et al (US 6376253 B1, Issued 4/2002, > 1 yr. before Applicant's earliest effective

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priority date (10/7/03); thus 102(b) art), teach isotopically enriching amino acid side chains with ^{13}C , ^{15}N , and ^2H (abstract, entire document), like the original genus presently claimed:

1. An amino acid wherein the sidechain of said amino acid is isotopically enriched with ^2H and wherein the backbone of said amino acid is isotopically enriched with an isotope selected from the group consisting of ^{13}C , ^{15}N , ^2H and any combination thereof, with the proviso that said amino acid is not isotopically enriched with ^2H at every hydrogen.

This same Anderson et al. reference is applied below as a 102(b)/103.

Claim Objections

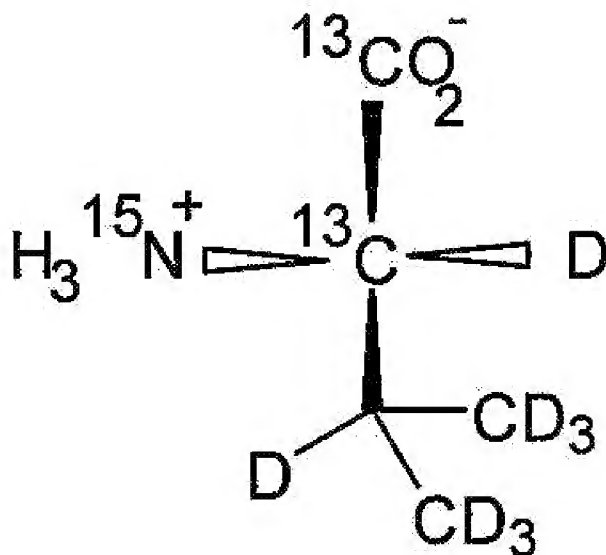
Claims 1, 3, and 6-11 are objected to because of the following informalities:

The claims have not been amended commensurate in scope with the elected invention of:

Compound chemical name & structure below:

$1, 2-^{13}\text{C}_2, ^{15}\text{N}, ^2\text{H}_8\text{-L-Valine}$

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Appropriate correction is required.

Claims 5-6 objected to because of the following informalities:

It is unclear what the difference in scope of the invention is between peptidic and peptide molecule. The specification was not found to provide clear guidance. Until this is clarified, a Double Patenting rejection for duplicate claim limitations is held in abeyance.

Appropriate correction is required.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3, and 6-11 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Anderson et al (US 6376253 B1, Issued 4/2002, > 1 yr. before Applicant's earliest effective priority date (10/7/03)).

Anderson et al. teach the isotopically enriching amino acid side chains with ¹³C, ¹⁵N, and ²H, including for the elected amino acid valine (abstract, entire document). By example therein:

Brief Summary Text - BSTX (13):

The goal of these methods has been to achieve universal and/or random isotopic enrichment of all of the amino acids of the protein. By contrast, some workers have described methods whereby certain residues can be relatively enriched in ¹H, ²H, ¹³C and ¹⁵N. For example, Kay et al., J. Mol. Biol., 263, 627-636 (1996) and Kay et al., J. Am. Chem. Soc., 119, 7599-7600 (1997) have described methods whereby isoleucine, alanine, valine and leucine residues in a protein may be labeled with ²H, ¹³

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C and ^{15}N , but specifically labeled with ^1H at the terminal methyl position. In this way, study of the proton-proton interactions between some of the hydrophobic amino acids may be facilitated. Similarly, a cell-free system has been described by Yokoyama et al., J. Biomol. NMR, 6(2), 129-134 (1995), wherein a transcription-translation system derived from E. coli was used to express human Ha-Ras protein incorporating ^{15}N serine and/or aspartic acid.

Detailed Description Text - DETX (19):

To prepare amino acids with simple alkyl sidechains, i.e., alanine, leucine, isoleucine, phenylalanine, methionine, and valine, the derivatized glycine molecule is treated with the appropriate alkyl halide to form the fully protected amino acid. For example, treating the derivatized glycine molecule with benzyl iodide leads to the formation of protected phenylalanine. A list of alkyl halides and corresponding amino acids is provided in Table 1.

##STR5##

Detailed Description Text - DETX (42):

Synthesis of (1,2- ^{13}C , ^{15}N , 2- ^2H) Valine

Detailed Description Text - DETX (62):

Synthesis of (1,2- ^{13}C , ^{15}N , 50% 2- ^2H) Valine

Detailed Description Text - DETX (74):

To one liter of CHO S SFM, serum-free media (Life Technologies), supplied by the manufacturer with amino acids, pyruvate and carbohydrate omitted (Catalog No. 0920261) at 37.degree. C. were added 212 mg (1,2- ^{13}C , ^{15}N , 50% 2- ^2H)leucine, 162 mg (1,2- ^{13}C , ^{15}N , 50% 2- ^2H)valine, and 188 mg of backbone labeled (1,2- ^{13}C , ^{15}N , 50% 2- ^2H)phenylalanine. The remaining unlabeled components were added as follows:

Detailed Description Paragraph Table - DETL (1):

TABLE 1 Alanine Me--I Isoleucine ##STR6## Leucine ##STR7## Methionine ##STR8## Phenylalanine ##STR9## Valine ##STR10##

Although Anderson et al. does not expressly teach the 'structure' including valine, valine is nevertheless taught as one of the amino acids for ^{13}C , ^{15}N , ^2H enrichment and thus is anticipated if not obvious.

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Similarly, the above in a “peptidic or peptide molecule”, if the same is not inherent within the compositions of Anderson et al., it is deemed wholly predictable as an obvious variation based merely on lexicography.

If not anticipated, then from the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 9/12/2010

/Maury Audet/
Primary Examiner, Art Unit 1654